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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,439	05/18/2001	Indra Prakash	2047.154	3715

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EXAMINER
ZUCKER, PAUL A

ART UNIT	PAPER NUMBER
1621	7

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/859,439	PRAKASH, INDRA	
	Examiner	Art Unit	
	Paul A. Zucker	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10,12,14 and 16-20* is/are rejected.

7)☒ Claim(s) *3,11,13 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Current Status

1. This action is responsive to Applicant's amendment of 29 March 2002 in Paper No 6.
2. Receipt and entry of Applicant's amendment is acknowledged.
3. The objections to the specification set forth in paragraph 1 of the previous Office Action in Paper No 4 are withdrawn in response to Applicant's amendment.
4. The objection to the abstract set forth in paragraph 2 of the previous Office Action in Paper No 4 is MAINTAINED in view of the fact that Applicant has not instructed entry of the amended abstract.
5. The objections to the claims set forth in paragraph 3 of the previous Office Action in Paper No 4 are MAINTAINED.
6. The rejections under 35 USC § 112, second paragraph, set forth in paragraphs 4-7 of the previous Office Action in Paper No 4 are withdrawn in response to Applicant's amendments and remarks.
7. Claims 1-20 remain outstanding.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1, 2, 4-10, 12, 14 and 16-20 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Burger et al (Chemmiker Zeitlung 1990, 114(7-8), pages 249-251) and further in view of Claude et al (US 5,510,508 04-1996).

Instantly claimed is a process for the synthesis of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl-L-phenylalanine-1-methyl ester (neotame) via: a) the formation of an oxazolidinone from N-[N-(3,3-dimethylbutyl)-L-α-aspartic acid from acarbonyl compound or its equivalent, followed by b) reacting the oxazolidinone with phenylalanine methyl ester to yield neotame.

Burger teaches (Page 250, left column, lines 17-34) the synthesis of oxazolidinones of general structure 3 (Page 249, upper right-hand column) which, with n=1 (compound 3a), corresponds to that derived from aspartic acid. The amino acid (100 mmol) in anhydrous dimethylsulfoxide is vigorously stirred at room temperature and a gaseous stream of hexafluoroacetone is introduced. The introduction of hexafluoroacetone is stopped when its uptake ceases and reflux is noted. Thus while Burger is silent with respect to the reactant ratios it reasonable to assume the instant claimed slight excess (1:1.1-1.4) of hexafluoroacetone is present. Reaction is continued for 2-3 hours to give the crystalline oxazolidinone after work-up. The Examiner notes that aspartic acid itself meets the limitation of an acid which serve as a catalyst to produce hexafluoroacetone hydrate. Burger further teaches (Page 250, last 5 lines of left column- first 9 lines of right column) the aminolysis of the oxazolidinones to form dipeptides such as aspartame. The oxazolidinone (20 mmol)

in anhydrous ether is slowly added with stirring at room temperature to a solution of phenylalanine methyl ester (24 mmol) in anhydrous ether (corresponding to 1:1.2 ratio of oxazolidinone:phenylalanine) and reaction continued for 24 hr to give a 72% yield of aspartame.

Burger is silent with respect to application of his process to the synthesis of neotame.

Claude, however, teaches (Column 1, lines 1-42) the structure of neotame, an artificial sweeter closely related in structure to aspartame. The closeness of the relationship between these two compounds is underscored by the fact that Claude further discloses (Column 3, line 63 – column 4, line 40) the synthesis of neotame in one step from aspartame.

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art. The motivation would have been to apply the efficient process disclosed by Berger for the synthesis of aspartame, a commercially important artificial sweetener, to the synthesis of the aspartame derivative, neotame. The expectation for success would be exceptionally strong because of the close structural similarities between aspartame and neotame.

Response to Applicant's Remarks with Regard to This Rejection

9. Applicant presents several arguments to which the Examiner responds below:

a. Applicant argues that Burger does not disclose the synthesis of oxazolidinone derivatives from N-alkyl-L-aspartic acid. The Examiner agrees with this and has not suggested otherwise in his rejection. Burger teaches the formation of the oxazolidinone derivative of L-aspartic acid itself. The instantly claimed process is simply the same process as that taught by Burger applied to an analogous starting material which produces the expected analogous product.

b. Applicant argues that Claude does not remedy the deficiencies of Burger since it teaches a different process for the synthesis of aspartame. The Examiner points out that Claude is relied upon only for his teaching of the structure of neotame as an aspartame derivative. Nothing more is required to suggest to one of ordinary skill in the art that the known process for the synthesis of aspartame as taught by Burger could be trivially modified to produce neotame.

c. Applicant further argues that aspartame and neotame have different properties such as solubility, melting point, pH stability, and impurity profile (which is not actually a property of a compound). The Examiner agrees that neotame and aspartame are different compounds. They are, however, analogs of each other and would be expected, by one of ordinary skill in the art, to show analogous behavior in the process taught by Burger. None of the differences in the physical properties enumerated by Applicant would lead one of ordinary skill in the art to expect different behavior in the process of Burger. Applicant's conclusion to that effect is in error.

Applicant's arguments filed 29 March 2002 have been fully considered but they are not persuasive for the reasons indicated above.

New Claim Objections

10. Claims 3, 11, 13 and 15 are finally objected to as being dependent upon a rejected base claim.

Conclusion

11. Claims 1-20 are outstanding. Claims 1, 2, 4-10, 12, 14 and 16-20 are finally rejected. Claims 3, 11, 13 and 15 are finally objected to.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker
Patent Examiner
Technology Center 1600

July 24, 2002

Johann Richter, Ph.D., Esq.
Supervisory Patent Examiner
Technology Center 1600